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Moya Kinnealey

Printed name of person mailing correspondence

Moya Kinnealey

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Junying Yuan *et al.*

Art Unit: 1617

Serial No.: 09/829,040

Examiner: Wang, Shengjun

Filed: April 9, 2001

Customer No.: 21559

Title: METHODS AND COMPOSITIONS FOR DECREASING CELL TOXICITY

Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

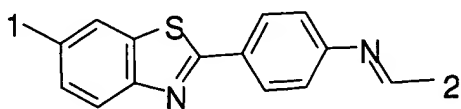
Kindly amend the claims as follows:

1. (Original) A method for decreasing cell death or toxicity, said method comprising the step of contacting a cell or an animal expressing an expanded polyglutamine repeat with diphenyldiazo-bis-alpha-naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof, in an amount sufficient to decrease said cell death or toxicity. .

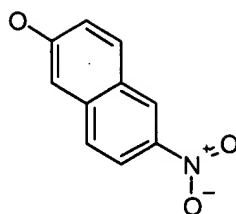
2. (Original) A method for decreasing aggregates or inclusions formed by expanded polyglutamine repeats in a cell or animal, said method comprising the step of contacting a cell or animal expressing an expanded polyglutamine repeat with diphenyldiazo-bis-alpha-naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof, in an amount sufficient to decrease said aggregates or inclusions.

3. (Original) The method of claim 1 or 2, wherein said expanded polyglutamine repeat is resistant to at least one of the compounds chosen from the group consisting of minocycline, daunomycin, rolitetracycline, Chrysamine G, iota-carrageenan, and dextran.

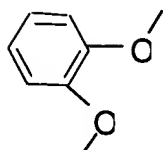
4. (Original) A method for decreasing cell death or toxicity, said method comprising the step of contacting a cell or an animal expressing an amyloidogenic protein with any of bromocriptine mesylate; haloperidol; nabumetone; primidone; hydrocortisone; phenazopyridine; R-(-)-deprenyl hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine; D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine methyl ether; a pharmaceutically effective derivative, salt, or isomer thereof; or a compound having the formula selected from any of:



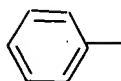
wherein 1 is CH<sub>3</sub> or H, and 2 is



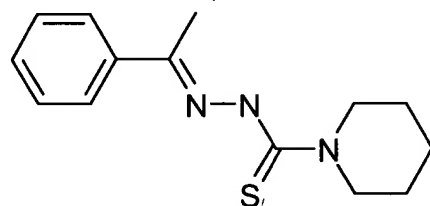
or wherein 1 is CH<sub>3</sub>, and 2 is



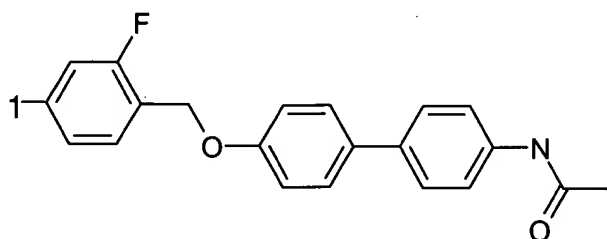
or wherein 1 is CH<sub>3</sub>, and 2 is



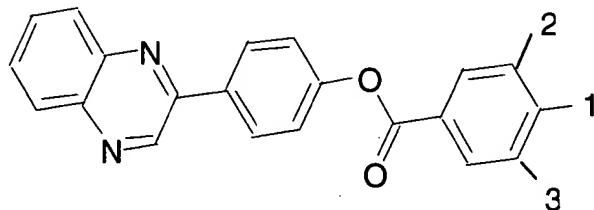
or a pharmaceutically effective derivative, salt, or isomer thereof;



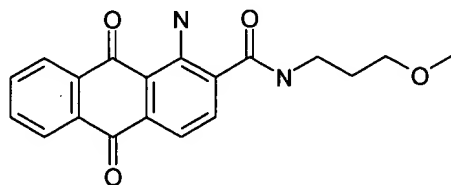
or a pharmaceutically effective derivative, salt, or isomer thereof;



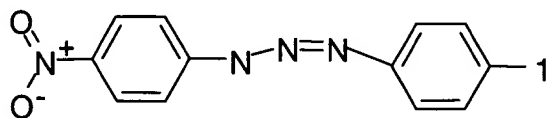
wherein 1 is H or NO<sub>2</sub><sup>-</sup>, or a pharmaceutically effective derivative, salt, or isomer thereof;



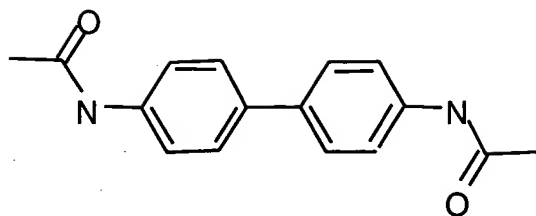
wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is NO<sub>2</sub>; or wherein 1 is Br, 2 is H, and 3 is NO<sub>2</sub>; or wherein 1 is Cl, 2 is H, and 3 is Br, or a pharmaceutically effective derivative, salt, or isomer thereof;



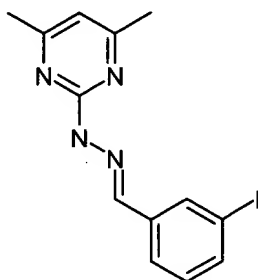
or a pharmaceutically effective derivative, salt, or isomer thereof;



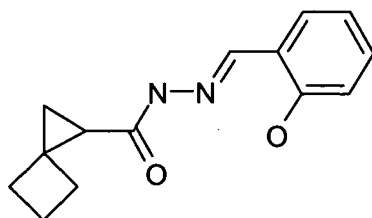
wherein 1 is NO<sub>2</sub>, Br, or O<sub>2</sub>, or a pharmaceutically effective derivative, salt, or isomer thereof;



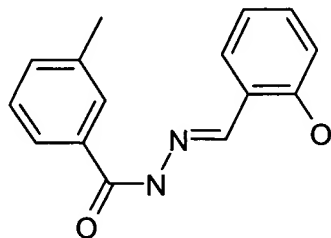
or a pharmaceutically effective derivative, salt, or isomer thereof



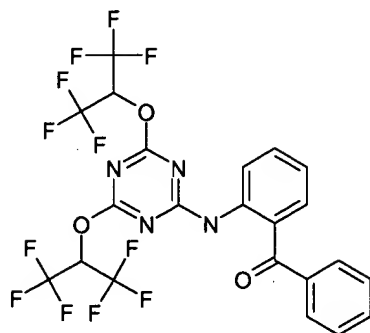
or a pharmaceutically effective derivative, salt, or isomer thereof;



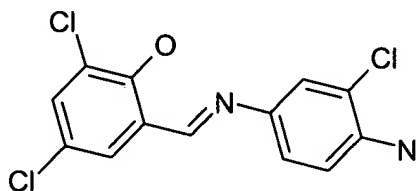
or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof;



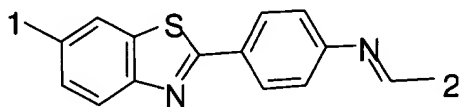
or a pharmaceutically effective derivative, salt, or isomer thereof; or



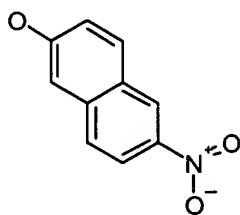
or a pharmaceutically effective derivative, salt, or isomer thereof, in an amount sufficient to decrease said cell death or toxicity, and wherein if said compound is haloperidol, phenazopyridine, or R-(-)-deprenyl, then said amyloidogenic protein is not beta-amyloid.

5. (Original) A method for decreasing aggregates or inclusions formed by an amyloidogenic protein in a cell or animal, said method comprising the step of contacting a cell or an animal expressing an amyloidogenic protein with any of bromocriptine mesylate; haloperidol; nabumetone; primidone; hydrocortisone; phenazopyridine; R-(-)-deprenyl hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine;

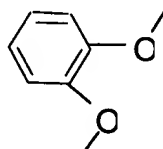
D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine methyl ether; a pharmaceutically effective derivative, salt, or isomer thereof; or a compound having the formula selected from any of:



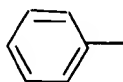
wherein 1 is CH<sub>3</sub> or H, and 2 is



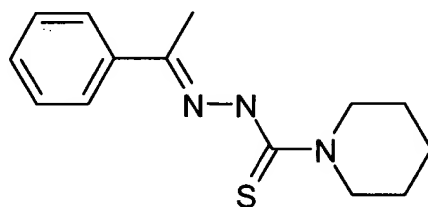
or wherein 1 is CH<sub>3</sub>, and 2 is



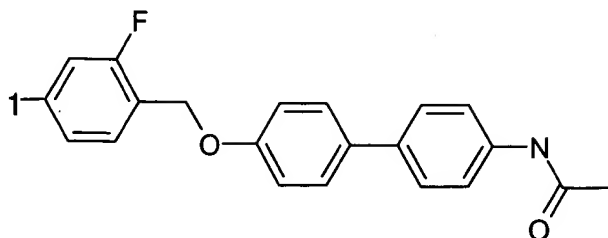
or wherein 1 is CH<sub>3</sub>, and 2 is



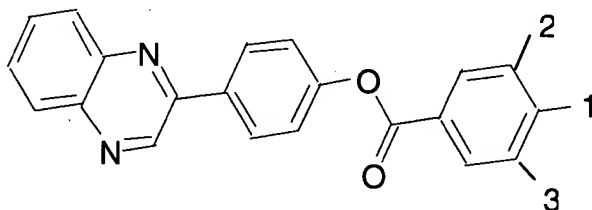
or a pharmaceutically effective derivative, salt, or isomer thereof;



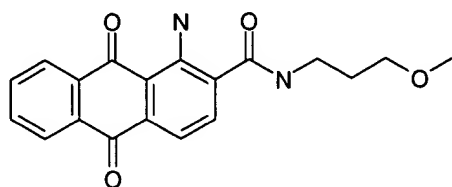
or a pharmaceutically effective derivative, salt, or isomer thereof;



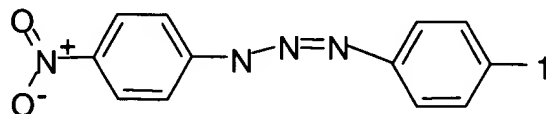
wherein 1 is H or NO<sub>2</sub><sup>-</sup>, or a pharmaceutically effective derivative, salt, or isomer thereof;



wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is NO<sub>2</sub>; or wherein 1 is Br, 2 is H, and 3 is NO<sub>2</sub>; or wherein 1 is Cl, 2 is H, and 3 is Br, or a pharmaceutically effective derivative, salt, or isomer thereof;

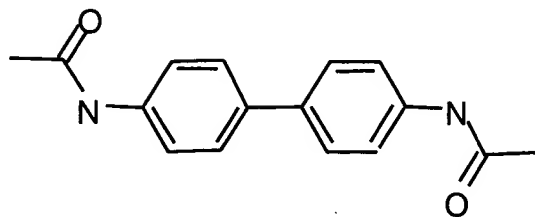


or a pharmaceutically effective derivative, salt, or isomer thereof;

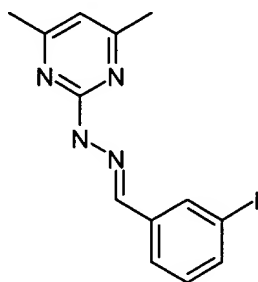




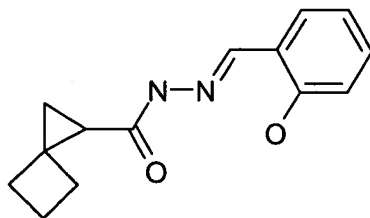
wherein 1 is NO<sub>2</sub>, Br, or O<sub>2</sub>, or a pharmaceutically effective derivative, salt, or isomer thereof;



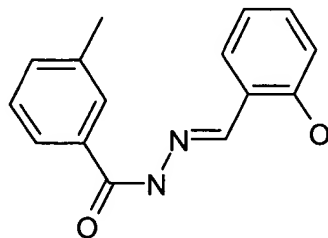
or a pharmaceutically effective derivative, salt, or isomer thereof



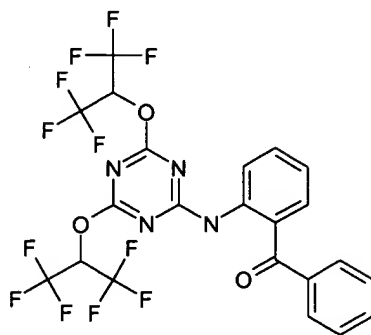
or a pharmaceutically effective derivative, salt, or isomer thereof;



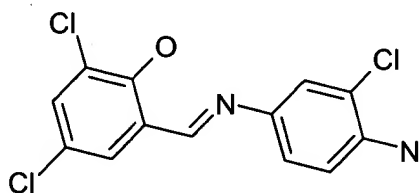
or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof; or

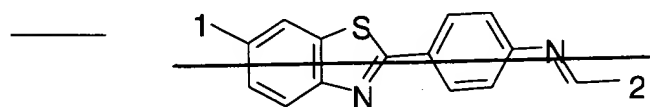


or a pharmaceutically effective derivative salt, or isomer thereof, in an amount sufficient to decrease said aggregates or inclusions, and wherein if said compound is haloperidol, phenazopyridine, or R-(-)-deprenyl, then said amyloidogenic protein is not beta-amyloid.

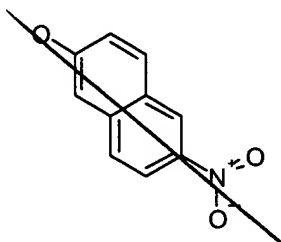
6. (Original) The method claim 1, 2, 4, or 5, wherein said cell is mammalian.
7. (Original) The method of claim 6, wherein said cell is human.
8. (Original) The method of claim 6, wherein said cell is a rodent cell.
9. (Original) The method of claim 6, wherein said cell is a germ-line cell.
10. (Withdrawn)
11. (Original) The method of claim 4 or 5, wherein said amyloidogenic protein is an expanded polyglutamine repeat.

12. (Currently amended) The A method of claim 1 or 2, wherein said animal is diagnosed as having for treating a condition; or a symptom associated with a condition, in a subject at risk for having an expressed expanded polyglutamine repeat, said method comprising administering diphenyldiazo bis-alpha-naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof, to said subject.

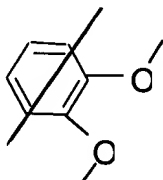
13. (Currently amended) The A method of claim 4 or 5, wherein said animal is diagnosed as having for treating a condition; or a symptom associated with a condition, in a subject at risk for having an expressed amyloidogenic protein, said method comprising administering any of bromocriptine mesylate; haloperidol; nabumetone; primidone; hydrocortisone; phenazopyridine; R(-) deprenyl hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine; D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine methyl ether; a derivative, salt, or isomer thereof; or a compound having the formula selected from the any of:

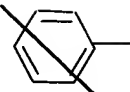


wherein 1 is CH<sub>3</sub> or H, and 2 is

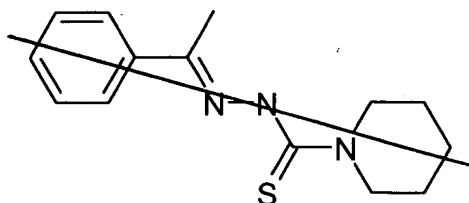


or wherein 1 is CH<sub>3</sub>, and 2 is

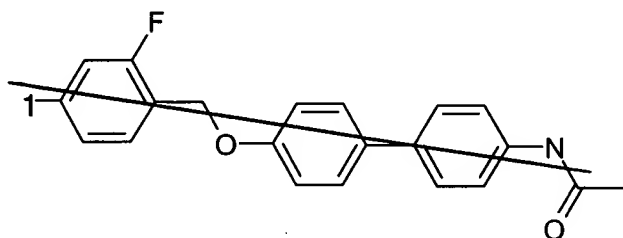


or wherein 1 is  $\text{CH}_3$ , and 2 is 

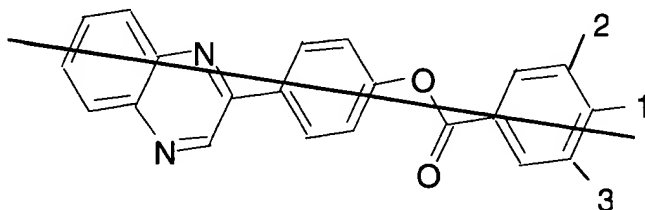
or a pharmaceutically effective derivative, salt, or isomer thereof;



*B<sup>1</sup>*  
*cont.*  
or a pharmaceutically effective derivative, salt, or isomer thereof;

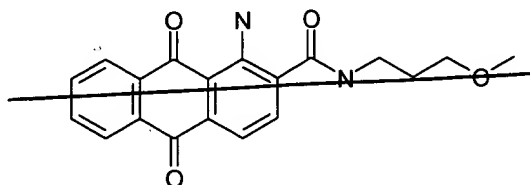


wherein 1 is H or  $\text{NO}_2$ , or a pharmaceutically effective derivative, salt, or isomer thereof;



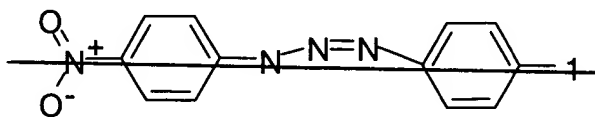
wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is  $\text{NO}_2$ ; or wherein 1

is Br, 2 is H, and 3 is NO<sub>2</sub>; or wherein 1 is Cl, 2 is H, and 3 is Br, or a pharmaceutically effective derivative, salt, or isomer thereof;

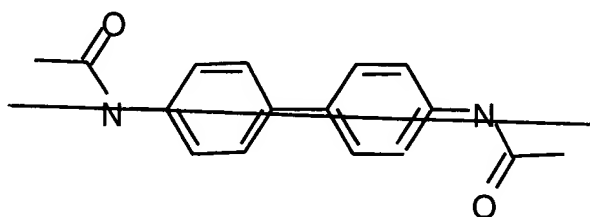


or a pharmaceutically effective derivative, salt, or isomer thereof;

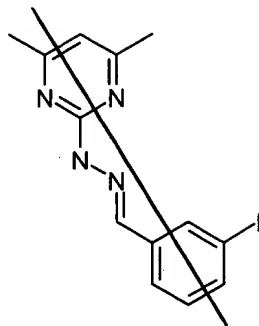
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cont.



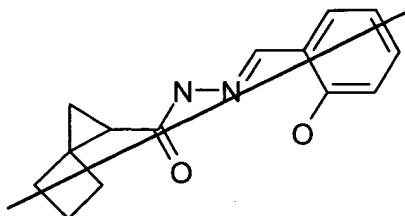
wherein 1 is NO<sub>2</sub>, Br, or O<sub>2</sub>, or a pharmaceutically effective derivative, salt, or isomer thereof;



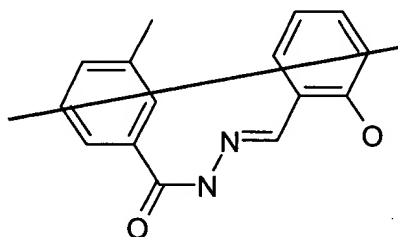
or a pharmaceutically effective derivative, salt, or isomer thereof



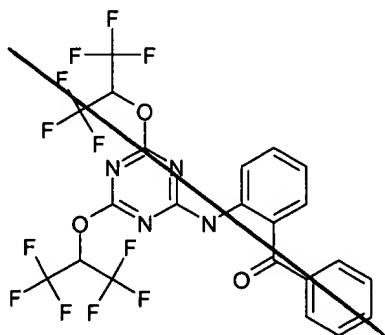
or a pharmaceutically effective derivative, salt, or isomer thereof;



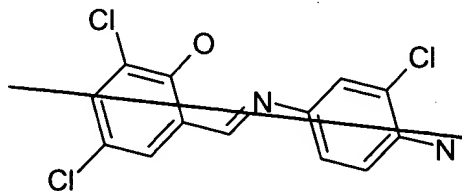
or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof; or



or a pharmaceutically effective derivative, salt, or isomer thereof to said subject.

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14. (Original) The method of claim 12 or 13, wherein said condition is a neurodegenerative disease.

15. (Original) The method of claim 14, wherein said neurodegenerative disease is any of Huntington's disease, spinobulbar muscular atrophy (SBMA), spino-cerebellar ataxia type 1, spino-cerebellar ataxia type 2, spino-cerebellar ataxia type 3, spino-cerebellar ataxia type 6, spino-cerebellar ataxia type 7, dentatorubral-pallidoluysian atrophy, or familial schizophrenia.

16. (Withdrawn)

17. (Cancelled)

R<sub>2</sub>  
18. (Currently amended) The method of claim 12 ~~or 17~~, wherein said condition is caused by expanded polyglutamine repeats.

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R<sub>3</sub>  
19. (Currently amended) The method of claim 12 or 13, wherein said animal subject is a mammal.

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20. (Currently amended) The method of claim 19, wherein said mammal subject is a human.

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21. (Original) The method of claim 12, wherein said expressed expanded polyglutamine repeat is resistant to at least one of the compounds chosen from the group consisting of minocycline, daunomycin, rolitetracycline, Chrysamine G, iota-carrageenan, or dextran.

22. (Original) The method of any of claims 1, 2, or 12, wherein said derivative is any one of Direct Orange 8, Direct Yellow 26, Direct Yellow 28, Direct Blue 158, Direct Orange 6, Direct Red 1, Direct Orange 1, or Direct Black 51.

23. (Original) The method of any of claims 1, 2, 4, or 5, wherein said animals is an animal diagnosed with, or having an increased likelihood of developing a neurodegenerative disease.

24. (Original) The method of claim 23, wherein said neurodegenerative disease is any of Huntington's disease, spinobulbar muscular atrophy (SBMA), spino-cerebellar ataxia type 1, spino-cerebellar ataxia type 2, spino-cerebellar ataxia type 3, spino-cerebellar ataxia type 6, spino-cerebellar ataxia type 7, dentatorubral-pallidoluysian atrophy, or familial schizophrenia.



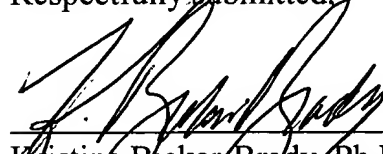
If there are any charges or any credits, please apply them to Deposit Account No.

03-2095.

Date:

March 14, 2003

Respectfully submitted,



Kristina Bieker-Brady, Ph.D.

Reg. No. 39,109

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



21559

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Certificate of Mailing: Date of Deposit: March 14, 2003

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Moya Kinnealey

Printed name of person mailing correspondence

Moya Kinnealey

Signature of person mailing correspondence

#9  
4/2/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Junying Yuan <i>et al.</i>	Art Unit:	1617
Serial No.:	09/829,040	Examiner:	Wang, Shengjun
Filed:	April 9, 2001	Customer No.:	21559
Title:	METHODS AND COMPOSITIONS FOR DECREASING CELL TOXICITY		

Commissioner for Patents  
Washington, D.C. 20231

REPLY TO RESTRICTION REQUIREMENT

In reply to the Restriction Requirement that was mailed in connection with the above-captioned case on December 17, 2002, applicant elects the invention of Group II, claims 1-9 and 11, and the species of diphenyldiazo-bis-alpha-naphthylaminesulfonate. The election is made with traverse.

Applicants respectfully request claims 12-15 and 18-24 be rejoined with the claims of Group II in view of the Preliminary Amendment submitted herewith. Applicants submit that the claims, as presently amended, fall within a single restriction group. Alternatively, Applicants submit that an examination of the entire application can be

performed without placing a serious burden on the Examiner.

The MPEP § 808.02 states:

Where, however, the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions.

In this regard, Applicants note that the Examiner has classified all of the claims into the same class and subclasses (class 514, subclasses 365, 252.12, 277, and 246). Thus, examination of all claims will not require a separate search. Accordingly, Applicants respectfully request rejoinder of all pending claims and examination of the entire application.

Enclosed is a petition to extend the time for replying for two months, to and including March 17, 2003. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:

*March 14, 2003*

*Kristina Bieker-Brady*  
\_\_\_\_\_  
Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,409

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045

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